IN THE SPECIFICATION:

Please amend the specification, as follows:

Page 1, lines 16-17:

Please substitute the following paragraph:

--US Patent Applications Serial Nos. 10/661,082, ..., 10/661,254 and 10/661,116 ~~(Atty Docket Nos. CC-0650, CC-0651, CC-0653, and CC-0654)~~, filed Sept. 12, 2003, contain subject matter related to that disclosed herein, all of which are incorporated by reference in their entirety.--

Page 3, line 25:

Please substitute the following paragraph:

--According to the present invention, a method of performing an assay process is provided comprising the steps of: providing microbeads in a solution; placing the microbeads on an alignment substrate; reading codes of the microbeads and the position thereof on the alignment substrate; reading the fluorescence on each microbead and the position thereof on the alignment substrate; and determining an assay result based on bead position and bead code of the earlier reading steps. The microbead may take the

form of an encoded particle that comprises: a particle substrate; at least a portion of the substrate being made of a substantially single material and having at least one diffraction grating embedded therein, the grating having a resultant refractive index variation within the single material at a grating location; and the grating providing an output optical signal indicative of a code when illuminated by an incident light signal propagating in free space, said output optical signal being a result of passive, non-resonant scattering from the grating when illuminated by the incident light signal.

The present invention also includes apparatus for reading microbeads that form part of an assay process, comprising: an alignment substrate for receiving the microbeads thereon: and a bead mapper for reading codes of the microbeads and the position thereof on the alignment substrate.--.

Page 7, lines 11-13:

Please delete the paragraph.

Page 14, lines 18-23:

Please substitute the following paragraph:

--Next, in step 46, the chip is provided to a Reader/Scanner 824 (Fig 3(a)) where the fluorescence of each of the functionalized/hybridized/reacted microbeads 72 is analyzed to determine information about the analyte reaction or hybridization for each bead and location. Next a step 47 determines the code 58 of each of the beads 72 from the information from the Bead Mapper, thereby determine which "target" analytes 52 - 54 are present in the solution 60. The assay results are provided in step 48.--.

Pages 16-17, Paragraph bridging pages:

Please substitute the following paragraph:

--For example, DNA probe molecules may be directly synthesized on the beads using standard phosphoramidite chemistry with no post synthetic purification, and the beads used as the solid support. The attachment to the bead may be done by preparing the beads using standard linker chemistry coated on the beads that allows the probe to attach to the bead. Then, the oligo probe may be grown base-by-base to create the oligo sequence. Alternatively, the entire desired oligo sequence may be pre-fabricated and then attached to the bead after fabrication. In that case,

the linker chemistry used on the bead would likely be different and possibly more complex than the linker chemistry used in direct synthesis. Also, the beads may be functionalized as discussed hereinbefore and then placed in a blocker solution of BSA Bovine Serum Albumin (or any other suitable blocker to prevent non-specific binding of the target molecule). The beads may then be hybridized by placing the beads in a hybridization solution. Any desirable hybridization solution may be used. One example is: 5x concentration of SSC (Standard Saline Citrate), 25% formamide, 0.1% SDS (Sodium Dodecyl Sulfate -soap - used to help the beads not stick to the walls of tube), a predetermined amount of complementary DNA (cDNA) to the sequence of a given Probe tagged with Cy3 fluorescent molecules, and a predetermined amount of complementary DNA (cDNA) to the sequence of that Probe tagged with Cy5 fluorescent molecules. Any other hybridization or analyte reaction technique may be used if desired.--

Pages 17-18, Paragraph bridging pages:

Please substitute the following paragraph:

--The "target" analytes 52 - 54 within the solution 60 are then mixed with the functionalized

microbeads 72 - 74. During the mixing of the "target" analytes 52 - 54 and the functionalized microbeads 72 - 74, the "target" analytes attach to the complementary probes 76 - 78, as shown for functionalized microbeads 72,73 having codes 12345678 and 34128913. Specifically, as shown in Fig. 6, "target" analytes 53 bonded with probes 76 of the functionalized microbeads 72 having the code 12345678, and "target" analytes 52 bonded with probes 77 of the functionalized microbeads 73 having the code 34128913. On the other hand, "target" analytes 54 did not bond with any probes, and ~~not~~ no "target" analytes 52 - 54 in the solution 60 bonded with probes 78 of the functionalized microbeads 74 having the code 11778154. Consequently, knowing which "target" analytes attach to which probes along with the capability of identifying each probe by the encoded microbead, the results of the assay would show that the unknown "target" analytes in the solution 60 includes "target" analytes 53, 54, as will be described in further detail.--.

Page 19, lines 1-3:

Please substitute the following paragraph:

--Referring to Figs. 7 and 8, then, each functionalized microbead 72 - 74 is read by a Bead Mapper 201 ~~20~~ to determine the identification code 58 of each of the functionalized microbeads and the location of each bead.--.

Page 19, lines 4-18:

Please substitute the following paragraph:

--Referring to Fig. 8, more specifically, as discussed herein and in the aforementioned patent applications, the codes in the microbeads 8 are detected when illuminated by incident light 24 from a code excite optical signal device 801 which produces a diffracted or output light signal 27 to a reader 820, which includes the optics and electronics necessary to read the codes in each bead 8, as described herein and/or in the aforementioned copending patent application. The reader 820 provides a signal on a line 822 indicative of the code in each of the bead 8 to a known computer ~~811~~ 812. The incident light 24 may be directed transversely from the side of the tray 84 (or from an end or any other angle) with a narrow band (single wavelength) and/or multiple wavelength source,

in which case the code is represented by a spatial distribution of light and/or a wavelength spectrum, respectively, as described hereinafter and in the aforementioned copending patent application. Other illumination, readout techniques, types of gratings, geometries, materials, etc. may be used for the microbeads 8, as discussed hereinafter and in the aforementioned patent application. The computer 811 provides an output signal on a line 813 indicative of the bead location and code.--.

Page 19, lines 19-21:

Please substitute the following paragraph:

--Referring to Figs. 8-10 ~~Fig. 9~~, the slide, tray or chip 84 is then placed in a reader or scanner 824 (also see Figs. (3(a)). The reader 824 reads each functionalized microbead 72 - 74 (Figs. 4-7) for fluorescence or other indicator of the analyte reaction.--.

Pages 19-20, Paragraph bridging pages:

Please substitute the following paragraph:

--In Fig. 7-10, a ~~A~~ light source 803 ~~(not shown)~~ may be provided to luminate the microbeads 72 - 74,

also shown as element 8 in Figs. 8-9. Once the fluorescent microbeads 72 - 74 are identified and knowing which probe 76 - 78 (or single strand of DNA) was attached to each coded, functionalized microbead 72 - 74, the bead detector 808 ~~20~~ determines which "target" analytes 52 -54 were present in the solution 60 (see Fig. 6). As described hereinbefore, the bead detector 808 ~~20~~ illuminates the functionalized microbeads 72 - 74 and focuses light 26 (Fig. 10) reflected by the diffraction grating 12 onto a CCD array or camera 61 ~~32~~, whereby the code 58 of the functionalized microbead 72 - 74 is determined. Secondly, the reader 824 includes a fluorescence detector 86 for measuring the fluorescence emanating from "target" analytes 52 - 54 attached to the probes 76 - 78. The scanner/reader 824 ~~fluorescence meter 86~~ includes a lens 804 ~~88~~ and optical fiber (not shown) ~~90~~ for receiving and providing the fluorescence from the "target" analyte 52 - 54 to the fluorescence meter or detector 808.--.

Page 20, lines 5-14:

Please substitute the following paragraph:

--Referring to Figs. 8-10 ~~Fig. 9~~, for assays that use fluorescent molecule markers to label or tag chemicals, an optical excitation signal 800 is incident on the microbeads 8 through the tray 84 and a fluorescent optical output signal ~~802~~ 806 emanates from the beads 8 that have the fluorescent molecule attached. The fluorescent optical output signal ~~802~~ 806 passes through a lens 804, which provides focused light 802 to a known optical fluorescence detector 808. Instead of or in addition to the lens ~~802~~ 804, other imaging optics may be used to provide the desired characteristics of the optical image/signal onto the fluorescence detector 808. The detector 808 provides an output signal on a line 810 indicative of the amount of fluorescence on a given bead 8, which can then be interpreted to determine what type of chemical is attached to the bead ~~10~~ 8.--.

Pages 20-21, Paragraph bridging pages:

Please substitute the following paragraph:

--The code signal 822 from the bead code reader 820 and the fluorescent signal 810 from the fluorescence detector are provided to a known computer 812. The computer reads the code associated with each

bead and determines the chemical probe that was attached thereto from a predetermined table that correlates a predetermined relationship between the bead code and the attached ~~probed~~ probes. In addition, the computer 812 reads the fluorescence associated with each bead and determines the sample or analyte that is attached to the bead from a predetermined data that correlates a predetermined relationship between the fluorescence tag and the analyte attached thereto. The computer 812 then determines information about the analyte and/or the probe as well as about the bonding of the analyte to the probe, and provides such information on a display, printout, storage medium or other interface to an operator, scientist or database for review and/or analysis, as indicated by a line 815.--.

Page 21, lines 3-20: [NEEDS AMENDMENT]

Please substitute the following paragraph:

--Generally, the assay of the present invention may be used to carry out any binding assay or screen involving immobilization of one of the binding agents. Such solid-phase assays or screens are well known in the chemical and biochemical arts. For example, such

screening may involve specific binding of cells to a molecule (e.g. an antibody or antigen) immobilized on a microbead in the assay followed by analysis to detect whether or to what extent binding occurs. Alternatively, the beads may subsequently removed from the groove plate for sorting and analysis via flow cytometry (see e.g. by Needels et al. (1993). Examples of biological compounds that may be assayed or screened using the assay of the present invention include, e.g. agonists and antagonists for cell membrane receptors, toxins, venoms, viral epitopes, hormones, sugars, cofactors, peptides, enzyme substrates, drugs inclusive of opiates and steroids, proteins including antibodies, monoclonal antibodies, antisera reactive with specific antigenic determinants, nucleic acids, lectins, polysaccharides, cellular membranes and organelles. In addition, the present invention may be used in any of a large number of well-known hybridization assays where nucleic acids are immobilized on a surface of a substrate, e.g. genotyping, polymorphism detection, gene expression analysis, fingerprinting, and other methods of DNA- or RNA-based sample analysis or diagnosis.--.

Pages 22-23, Paragraph bridging pages:

Please substitute the following paragraph:

--Some current techniques used in combinatorial chemistry or biochemistry are described in US Patent No. 6,294,327, entitled "Apparatus and Method for Detecting Samples Labeled With Material Having Strong Light Scattering Properties, Using Reflection Mode Light and Diffuse Scattering", issued Sept. 23, 2001 to Walton et al.; US Patent No. 6,242,180, entitled "Computer Aided Visualization and Analysis System for Sequence Evaluation", issued June 5, 2001, to Chee; US Patent No. 6,309,823 entitled "Arrays of Nucleic Acid Probes for Analyzing Biotransformation of Genes and Methods of Using the Same", Oct. 30, 2001, to Cronin et al.; US Patent No. 6,440,667, entitled "Analysis of Target Molecules Using an Encoding System"; US Patent No. 6,355,432, entitled "Products for Detecting Nucleic Acids"; US Patent No. 6,197,506, entitled "Method of Detecting Nucleic Acids"; US Pat No. 6,309,822, entitled "Method for comparing copy number of nucleic acid sequences"; US Patent No. 5,547,839, entitled "Sequencing of surface immobilized polymers utilizing micro- fluorescence detection", US Patent No. 6,383,754, entitled "Binary Encoded Sequence

Tags", and US Patent ~~No. 6,383,754~~ Nos. 6,261,782 and 6,667,121, entitled "Fixed Address Analysis of Sequence Tags", which are all incorporated herein by reference to the extent needed to understand the present invention.--.

Page 24, lines 4-12:

Please substitute the following paragraph:

--Referring to Fig. 10, ~~The~~ the reflected light 27, comprises a plurality of beams 26-36 that pass through a lens 37, which provides focused light beams 46-56, respectively, which are imaged onto a CCD camera 61 ~~60~~. The lens 37 and the camera 61 ~~60~~, and any other necessary electronics or optics for performing the functions described herein, make up the reader/detector 808 ~~reader 29~~. Instead of or in addition to the lens 37, other imaging optics may be used to provide the desired characteristics of the optical image/signal onto the camera 61 ~~60~~ (e.g., spots, lines, circles, ovals, etc.), depending on the shape of the substrate 10 and input optical signals. Also, instead of a CCD camera other devices may be used to read/capture the output light.--.

Page 27, lines 17-21:

Please substitute the following paragraph:

--Referring to Fig.13, illustrations (a)-(c), for the grating 12 in a cylindrical substrate 10 having a sample spectral 17 bit code (i.e., 17 different pitches Λ1-Λ17), the corresponding image on the CCD (Charge Coupled Device) camera 60 is shown for a digital pattern 89 of 7 bits turned on (10110010001001001); 9 bits turned on of (11000101010100111); and all 17 bits turned on of (11111111111111111).--

Page 30, lines 1-7:

Please substitute the following paragraph:

--Referring to Fig. 16, illustration (b), the transmission wavelength spectrum of the transmitted output beam 330 (which is transmitted straight through the grating 12) will exhibit a series of notches (or dark spots) 696. Alternatively, instead of detecting the reflected output light 310, the transmitted light 330 may be detected at the detector/reader 308. It should be understood that the optical signal levels for the reflection peaks 695 and transmission notches 696 will depend on the "strength" of the grating 12,

i.e., the magnitude of the index variation n in the grating 12.--.

Pages 30-31, Paragraph bridging pages:

Please substitute the following paragraph:

--Alternatively, the source 300 may provide a continuous broadband wavelength input signal such as that shown as a graph 316. In that case, the reflected output beam 310 signal is provided to a narrow band scanning filter 318 through a lens 321 which scans across the desired range of wavelengths and provides a filtered output optical signal 320 to the reader 308. The filter 318 provides a sync signal on a line 322 to the reader, which is indicative of which wavelengths are being provided on the output signal 320 to the reader and may be similar to the sync signal discussed hereinbefore on the line 306 from the source 300. In this case, the source 300 does not need to provide a sync signal because the input optical signal 24 is continuous. Alternatively, instead of having the scanning filter being located in the path of the output beam 310, the scanning filter may be located in the path of the input beam 24 as indicated by the

dashed box 324, which provides the sync signal on a line 323.---.

Page 32, lines 7-12:

Please substitute the following paragraph:

--In this case, rather than having the input light 24 coming in at the conventional Bragg input angle θi, as discussed hereinbefore and indicated by a dashed line 701, the grating 12 is illuminated with the input light 24 oriented on a line 705 orthogonal to the longitudinal grating vector 704 ~~705~~. The input beam 24 will split into two (or more) beams of equal amplitude, where the exit angle θ_o can be determined from Eq. 1 with the input angle $\theta_i=0$ (normal to the longitudinal axis of the grating 12).---.

Page 32, lines 13-19:

Please substitute the following paragraph:

--In particular, from Eq. 1, for a given grating pitch $\Lambda 1$, the +/-1st order beams (m=+1 and m=-1) ~~,~~ corresponds to output beams 700,702, respectively. The ~~For the~~ +/-2nd order beams (m=+2 and m=-2) ~~,~~ corresponds to output beams 704,706, respectively. The

0^{th} order (undiffracted) ~~(undefracted)~~ beam (m=0) ~~,~~ corresponds to beam 708 and passes straight through the substrate. The output beams 700-708 project spectral spots or peaks 710-718, respectively, along a common plane, shown from the side by a line 709, which is parallel to the upper surface of the substrate 10.--.

Page 35, lines 7-20:

Please substitute the following paragraph:

--Referring to Fig. 21, instead of using an optical binary (0-1) code, an additional level of multiplexing may be provided by having the optical code use other numerical bases, if intensity levels of each bit are used to indicate code information. This could be achieved by having a corresponding magnitude (or strength) of the refractive index change (δn) for each grating pitch Λ. Four intensity ranges are shown for each bit number or pitch Λ, providing for a Base-4 code (where each bit corresponds to 0,1,2, or 3). The lowest intensity level, corresponding to a 0, would exist when this pitch Λ is not present in the grating 12. The next intensity level 450 would occur when a

first low level δn1 exists in the grating that provides an output signal within the intensity range corresponding to a 1. The next intensity level 452 would occur when a second higher level δn2 exists in the grating 12 that provides an output signal within the intensity range corresponding to a 2. The next intensity level 454 ~~452~~, would occur when a third higher level δn3 exists in the grating 12 that provides an output signal within the intensity range corresponding to a 3.--.

Page 37, lines 7-20:

Please substitute the following paragraph:

--Referring to Fig. 23, if the value of n1 in the grating region 20 is greater than the value of n2 in the non-grating region 18, the grating region 20 of the substrate 10 will act as a known optical waveguide for certain wavelengths. In that case, the grating region 20 acts as a "core" along which light 630 is guided and the outer region 18 acts as a "cladding" which helps confine or guide the light. Also, such a waveguide will have a known "numerical aperture" (θna) that will allow light that is within the aperture θna

to be directed or guided along the grating axis 207 and reflected axially off the grating 12 and returned and guided along the waveguide. In that case, the grating 12 will reflect light 631 having the appropriate wavelengths equal to the pitches Λ present in the grating 12 back along the region 20 (or core) of the waveguide, and pass the remaining wavelengths of light as the light 632. Thus, having the grating region 20 act as an optical waveguide for wavelengths reflected by the grating 12 allows incident light that is not aligned exactly with the grating axis 207 to be guided along and aligned with the grating 12 axis 207 for optimal grating reflection.--.

Pages 42-43, Paragraph bridging pages:

Please substitute the following paragraph:

--Referring to Fig. 33, illustrations (a), (b), (c), (d), and (e) the substrate 10 may have one or more holes located within the substrate 10. In illustration (a), holes 560 may be located at various points along all or a portion of the length of the substrate 10. The holes need not pass all the way through the substrate 10. Any number, size and spacing for the holes 560 may be used if desired. In

illustration (b), holes 572 may be located very close together to form a honeycomb-like area of all or a portion of the cross-section. In illustration (c), one (or more) inner hole 566 may be located in the center of the substrate 10 or anywhere inside of where the grating region(s) 20 are located. The inner hole 566 may be coated with a reflective coating 573 to reflect light to facilitate reading of one or more of the gratings 12 and/or to reflect light diffracted off one or more of the gratings 12. The incident light 24 may reflect off the grating 12 in the region 20 and then reflect off the surface 573 to provide output light 577. Alternatively, the incident light 24 may reflect off the surface 573, then reflect off the grating 12 and provide the output light 575. In that case the grating region 20 may run axially or circumferentially 571 around the substrate 10. In illustration (d), the holes 579 may be located circumferentially around the grating region 20 or transversely across the substrate 10. In illustration (e), the grating 12 may be located circumferentially around the outside of the substrate 10, and there may be holes 574 inside the substrate 10. In operation, the incident light 24 may reflect

off the surface, then reflect off the grating 12 and provide the output light 576.--.

Page 43, lines 16-18:

Please substitute the following paragraph:

--Referring to Fig. 36, at least a portion of a side of the substrate 10 may be coated with a reflective coating 514 to allow incident light 510 to be reflected back to the same side from which the incident light came, as indicated by reflected light 512.--.

Page 43, lines 19-29:

Please substitute the following paragraph:

--Referring to Fig. 37, illustrations (a) and (b), alternatively, the substrate 10 can be electrically and/or magnetically polarized, by a dopant or coating, which may be used to ease handling and/or alignment or orientation of the substrate 10 and/or the grating 12, or used for other purposes. Alternatively, the bead may be coated with conductive material, e.g., metal coating on the inside of a holey ~~holy~~ substrate, or metallic dopant inside the substrate. In these cases, such materials can cause

the substrate 10 to align in an electric or magnetic field. Alternatively, the substrate can be doped with an element or compound that fluoresces or glows under appropriate illumination, e.g., a rare earth dopant, such as Erbium, or other rare earth dopant or fluorescent or luminescent molecule. In that case, such fluorescence or luminescence may aid in locating and/or aligning substrates.--.

Page 44, lines 1-5:

Please substitute the following paragraph:

--Referring to Fig. ~~fig.~~ 3(a), instead of the Bead Mapper providing the code and position information directly to the Reader/scanner 824, it may provide this data to an Assay Analysis device 901, which may also received the bead fluorescence or analyte reaction information and position from the reader/scanner 824. The assay analyzer can then provide the assay results as discussed hereinbefore for the reader/scanner.--.

Page 45, lines 10-13:

Please substitute the following paragraph:

--As shown, the microbead elements 8 are placed in the tray 200 with grooves 205 to allow the elements 8 to be aligned in a predetermined direction for illumination and reading/detection as discussed herein. Alternatively, the grooves 205 may have holes 210 that provide suction to keep the elements 8 in position. In operation, in response to incident light 212 provided perpendicular to the plane of the tray 200, the element 8 reflects light 214; while in response to incident light 216 provided oblique to the plane of the tray 200, the element 8 reflects light 218.--

Page 47, lines 9-15:

Please substitute the following paragraph:

--Referring to Fig. 41, an alternative embodiment, wherein the groove plate discussed hereinbefore with Fig. 38 may be used for the end illumination/readout condition. As shown, the beads 8 are arranged in V-grooves 205, while may also take the form of square grooves generally indicated as dashed lines 211. In this case, the grating 12 may have a blaze angle such that light incident 699 along the axial grating axis will be reflected upward as

reflected light 683, downward as reflected light 681, or at a predetermined angle for code detection. Similarly, the input light 697 may be incident on the grating in a downward, upward, or at a predetermined angle and the grating 12 may reflect light along the axial grating axis for code detection.--.

Page 52, lines 1-7:

Please substitute the following paragraph:

--Fig. 50(b) shows an alternative embodiment of a rotating disk generally indicated as 1200, having a disk platform 1202 with planar groove plates 1204a, b, c, d, e, f that are shown with grooves oriented in any one or more different ways. One or more of the planar groove plates 1204a, b, c, d, e, f may have an optional channel 1206, 1208 for fluid run-off, as shown, and a barrier for preventing the microbeads from flying off the plate. As shown, the window 1262 for reading the beads is in contact with the fluid containing the beads.--.